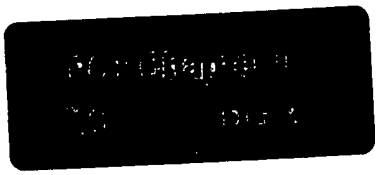
IN THE WORLD INTELLECTUAL PROPERTY OFFICE

In The Matter of International Patent Application:

Applicant	:	**University of Guelph; et al.**
PCT Application No.	:	**PCT/CA00/00305**
PCT Filing Date	:	**March 24, 2000**
Title	:	**Micropropagation And Preparation Of Phytopharmaceutical Plants**
Our File	:	**O8-882993WO**
Date	:	**March 19, 2001**

European Patent Office
Erhardstrasse 27
D-80331 Munich
FEDERAL REPUBLIC OF GERMANY



Article 34 Amendment

Dear Sir:

This is in response to the Office Letter dated December 18, 2000.

IN THE CLAIMS

Claims 1-61: Cancel without prejudice, and replace therefor with new claims 1-48. Applicant reserves the right to insert any one of these cancelled claims should this be required in the future

REMARKS

For the ease of identifying claims within the present set of claims, please note that:

Old	New
claim 1	claim 49;
claims 2-36	claims 5-39;
claim 37	claim 2;
claims 38-44	claims 5-11;
claim 45	claim 44;
claim 46	claims 1 and 45;
claim 47	claim 5;
claim 48	claim 4;
claim 49	claim 40;
claim 50	claim 41;
claim 51	claim 42;
claims 52-54	claims 10-12;
claim 55	claim 19;
claim 56	claim 16;
claim 57	claim 47;
claim 58	claim 3;
claim 59	claim 5;
claim 60	claim 4;
claim 61	claim 48.

New claim 49 (corresponding to old claim 1) has been amended to indicate that the method for *in vitro* propagation results in *de novo* shoot formation of non-meristematic tissue. Support for this amendment can be found throughout the specification, for example page 23, last paragraph; page 25, last paragraph; page 34, first paragraph; and page 37, last paragraph. Furthermore, each of the plants propagated using the method of claim 49 have involved non-meristematic tissue for example, hypocotyl, petiole, epicotyl, stem leaf or shoot tissues. For example, propagation of St. John' Wart in Example 1 involves the use of hypocotyl sections as indicated on page 33, the first paragraph of Example 1. Micropropagation of Echinacea in Example 2 has been performed using petiole explants as indicated in the middle of page 37. Micropropagation of Huang-qin has been obtained using hypocotyls as indicated in the last paragraph of page 42 to the top of page 43, as well as epicotyls as indicated on page 44 through to page 45. In Example 4, the micropropagation of feverfew is described using stem, leaf, and shoot explants as indicated on the second paragraph on page 46.

D1 (Sojakowska and Kisiel) disclose obtaining shoot cultures from nodal stem explants. As one of skill in the art would realize, nodal stem explants are meristematic in origin and the micropropagation of such explants does not result in *de novo* shoot formation, but rather inducing budbreak of existing meristematic tissues. Similarly in D2 (Shetty) the use of shoot apex explants as in Example 2 (column 11, line 24, and lines 36 through to 44) as well as the use of apical buds as indicated in Example 3, column 15, lines 47 through to 50. In D3 (Banerjee) there is no teaching of subculturing the explants on growth regulator free basal media as required in claim 49. Applicant therefore submits that any one or a combination of D1 to D3 do not disclose or suggest a method of *in vitro* micropropagation of the phytopharmaceutical plants that involves *de novo* shoot formation of non-meristematic tissue in the presence of a growth regulator having cytokinin activity, followed by transferring the regenerated tissue to a basal medium. Therefore Applicant submits that new claim 49 is free of the prior art.

Respectfully submitted

GOWLING LAFLEUR HENDERSON LLP

Agents for Applicant
Konrad A . Sechley, Ph.D.
KAS:bsl
Enclosures.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A method for the *in vitro* micropropagation and phytofortification of a phytopharmaceutical plant comprising:

a) culturing a sterile explant of said phytopharmaceutical plant on an induction medium comprising at least one plant growth regulator having cytokinin activity, to form regenerated tissue;

b) transferring said regenerated tissue to a basal medium and culturing to form plantlets; and

c) subculturing said plantlets onto a basal medium containing at least one additive of interest, to allow uptake and accumulation of said at least one additive of interest in a bio-available form in said plantlet.

2. The method of claim 1, wherein after said step of culturing (step a)), and prior to said step of transferring (step c)), said regenerated tissue is placed on a basal medium and subcultured to allow optimized formation of regenerated tissue; and

3. The method of claim 1 wherein after said step of transferring (step b)), said plantlet is transferred to a hydroponic environment with a recycling solution containing at least one additive of interest to allow uptake and accumulation of said at least one additive of interest in a bioavailable form within said plantlet or seedling.

4. The method according to any one of claim 1, 2 or 3, wherein in said culturing step, said at least one additive of interest is selected from boron, calcium, chloride, chromium, cobalt, copper, iron, lithium, iodine, magnesium, manganese, molybdenum, nickel, phosphorous, potassium, selenium, silicon, sodium, sulphur, tin, vanadium and zinc.

5. The method of any one of claims 1 to 4, wherein said phytopharmaceutical plant is selected from the group consisting of:

Achillea millefolium

Achyranthes bidentata

Aconitum napellus

Adonis aestivalis

Agastache mexicana

Agrimonia eupatoria

Agathosma betulina

Allium sp

Anchusa officinalis

Anemopsis californica

Angelica dahurica

Angelica polymorpha sinensis (A. sinensis)

Arnica Montana

Ammi visnaga

Arctostaphylos uva-ursi

Asclepias tuberosa

Astragalus membranaceus

Astragalus chinensis

Baphicacanthus cusia

Bixa orellana

Bupleurum falcatum

Brugmansia (Datura) spp.

Campanula rapunculus

Carum roxburgianum

Carum copticum

Cassia tora

Chamaelirium luteum

Chimaphila umbellata

Commiphora africana

Conium maculatum

Crithium maritimum

Datura metel (Datura alba)

Datura inoxia

Dracocephalum moldavica

Echinacea sp.

Eclipta alba (E[redacted]strata)

Ephedra nevadensis

Eriodictyon californicum

Eucommia ulmoides

Eupatorium perfoliatum

Filipendula vulgaris (F. hexapetala)

Gaultheria procumbens

Geum urbanum

Houttuynia cordata

Hydrocotyle asiatica (Centella asiatica)

Hypericum perforatum cv. Anthos

Inula helenium

Jatropha curcas

Leptospermum scoparium

Lespedeza capitata

Ligusticum porteri

Ligustrum lucidum

Lithospermum officinale

Lycium barbarum

Mucuna pruriens

Mandragora officinarum

Origanum dictamnus

Parietaria judaica (P. officinalis)

Phyllanthus emblica

Picrasma excelsa

Piniella ternate

Pogostemon patchouli

Polygonum multiflorum

Porophyllum ruderale ssp. macrocephalum

Prunella vulgaris

Pueraria lobata (P. thunbergiana)

Rauvolfia serpentina

Rivea corymbosa

Sanguinaria Ca[redacted]nsis

Satureja douglasii

Schizonepeta tenuifolia

Scutellaria baicalensis

Solanum xanthocarpum (S. surattense)

Sutherlandia frustescens

Tabebuia impetiginosa

Tanacetum parthenium

Tribulus terrestris

Trichosanthes kirilowii

Turnera diffusa

Voacanga africana, and

Withania somnifera

6. The method according to claim 5, wherein said phytopharmaceutical plant is selected from St. John's wort (*Hypericum perforatum* cv. Anthos), Huang-qin (*Scutellaria baicalensis*), *Echinacea sp.* and feverfew (*Tanacetum parthenium*).

7. The method according to any one of claims 1 to 6, wherein said at one plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron (TDZ, *N*-phenyl-*N'*-(1,2,3-thidiazol-yl)urea), benzylaminopurine (BAP), zeatin, CPPU (N-(2-chloro-4pyridyl)-N(-phenyl urea) and 2-*i*-P (N6-(2-isopentenyl) adenine or 6-gamma,gamma-dimethylallylamino purine).

8. The method according to claim 7, wherein said at least one plant growth regulator having cytokinin activity is selected from thidiazuron (TDZ) and benzylaminopurine (BAP).

9. The method according to claim 8, wherein said induction medium comprises from about 0.001 to about 25 μmol•L^{-1} of said at least plant growth regulator having cytokinin activity.

10. The method according to claim 8, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

11. The method according to any one of claims 1 to 10, wherein said explant is selected from the seed, petiole, hypocotyl, stem, cotyledon and leaf.

12. The method according to any one of claims 1 to 4, wherein said phytopharmaceutical plant is St. John's wort.

13. The method according to claim 12, wherein said plant growth regulator having cytokinin activity is thidiazuron.

14. The method according to claim 13, wherein the induction medium comprises thiadiazuron from about 0.001 to about 25 $\mu mol \cdot L^{-1}$.

15. The method according to claim 14, wherein the induction medium comprises thiadiazuron from about 4 to about10 $\mu mol \cdot L^{-1}$.

16. The method according to claim 12, wherein said sterile explant is maintained on said induction medium from about 1 to about 15 days.

17. The method according to claim 16, wherein said sterile explant is maintained on said induction medium from about 8 to about 10 days.

18. The method according to claim 12, wherein said explant is etiolated hypocotyl.

19. The method according to any one of claims 1 to 4, wherein the phytopharmaceutical plant is *Echinacea sp.*.

20. The method according to claim 19, wherein said plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron and benzylaminopurine.

21. The method according to claim 20, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said plant growth regulator having cytokinin activity.

22. The method ac[redacted]ng to claim 20, wherein said plant gr[redacted] regulator having cytokinin activity is from about 1.0 to about 15 μmol•L^{-1}.

23. The method according to claim 19, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

24. The method according to claim 23, wherein said sterile explant is maintained on said induction medium from about 10 to about 35 days.

25. The method according to claim 19, wherein said explant is petiole.

24. The method according to any one of claims 1 to 4, wherein said phytopharmaceutical plant is Huang qin.

27. The method according to claim 26, wherein said plant growth regulator having cytokinin activity is thidiazuron.

28. The method according to claim 27, wherein said induction medium comprises from about 0.001 to about 25 μmol•L^{-1} of said plant growth regulator having cytokinin activity.

29. The method according to claim 28, wherein said plant growth regulator having cytokinin activity is from about 1.5 to about 20 μmol•L^{-1}

30. The method according to claim 26, wherein said sterile explant is maintained on said induction medium from about 1 to about 30 days.

31. The method according to claim 30, wherein said sterile explant is maintained on said induction medium from about 14 to about 20 days.

32. The method according to claim 26, wherein said explant is selected from seeds, hypocotyl and stems.

33. The method according to any one of claims 1 to 4, where the phytopharmaceutical plant is feverfew.

34. The method according to claim 33 wherein said plant growth regulator having cytokinin activity is thidiazuron.

35. The method according to claim 34, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said plant growth regulator having cytokinin activity.

36. The method according to claim 35, wherein said plant growth regulator having cytokinin activity is from about 2.0 to about 8.0 $\mu mol \cdot L^{-1}$

37. The method according to claim 33, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

38. The method according to claim 37, wherein said sterile explant is maintained on said induction medium from about 20 to about 35 days.

39. The method according to claim 33, wherein the explant is selected from leaf, stem, petiole and hypocotyl.

40. The method according to claim 4, wherein said at least one additive of interest is zinc.

41. A method according to claim 4, wherein said at least one additive of interest is lithium.

42. The method according to claim 4, wherein said at least one additive of interest within said basal medium, is from about 0.001 to about 500 $mg \cdot L^{-1}$.

44. The method according to claim 2, wherein, in said transferring step, said regenerated tissue is subcultured for about 1 to about15 days.

45 A method for p[redacted]fortification of an *in vitro*-grown phy[redacted]rmaceutical plant comprising:

a) culturing a sterile seedling, explant or regenerated tissues to form a plantlet; and

b) subculturing said plantlet onto a basal medium containing at least one additive of interest, to allow uptake and accumulation of said at least one additive of interest in a bio-available form in said plantlet.

46. The method according to claim 45, wherein, in said step of culturing, said plantlets are produced either:

a) on a sterile explant of said phytopharmaceutical plant grown on an induction medium comprising at least one plant growth regulator having cytokinin activity, or

b) grown from a sterile seed, or

c) seedling in culture.

47. The method according to claim 46, wherein said at one plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron (TDZ, *N*-phenyl-*N'*-(1,2,3-thidiazol-yl)urea), benzylaminopurine (BAP), zeatin, CPPU (N-(2-chloro-4pyridyl)-N(-phenyl urea) and 2-*i*-P (N6-(2-isopentenyl) adenine or 6-gamma,gamma-dimethylallylamino purine).

48. A phytopharmaceutical plant prepared by the method of any one claims 1 to 4, or 45 to 47 and comprising an elevated level of said additive of interest when compared to a plant grown in the absence of said additive of interest.

49. A method for the *in vitro* micropropagation involving *de novo* shoot formation of non-meristematic tissue of a phytopharmaceutical plant comprising:

a) culturing a sterile explant of said phytopharmaceutical plant on an induction medium comprising one or more plant growth regulators having cytokinin activity, to form regenerated tissue; and

b) transferring said regenerated tissue to a basal medium and culturing to form plantlets.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
08-882993WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00305	24/03/2000	25/03/1999
International Patent Classification (IPC) or national classification and IPC A01H4/00		
Applicant UNIVERSITY OF GUELPH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/10/2000	
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Van Woensel, G Telephone No. +49 89 2399 2089

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00305

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-55	as originally filed				

Claims, No.:

1-49	as received on	21/03/2001	with letter of	19/03/2001	

Drawings, sheets:

1/12-12/12	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   ☐ the language of publication of the international application (under Rule 48.3(b)).
   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.
   ☐ filed together with the international application in computer readable form.
   ☐ furnished subsequently to this Authority in written form.
   ☐ furnished subsequently to this Authority in computer readable form.
   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:
   ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 49.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 49.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-47

	No:	Claims	48
Inventive step (IS)	Yes:	Claims	1-47
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-48
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Ad V

Reference is made to the following document:

D1: STOJAKOWSKA, A.: 'Production of parthenolide in organ cultures of feverfew' PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973

1. The subject-matter of claim 1 meets the requirements of Article 33 PCT: Document D1 discloses a method for the in vitro propagation of *Tanacetum parthenium* comprising, culturing a sterile explant of said plant on an induction medium comprising 6-benzylaminopurine and transferring said regenerated tissue to a basal medium and culturing to form plantlets.

1.1 Document D1 does not disclose that the plantlets are subcultured onto a basal medium containing at least one additive of interest to allow uptake and accumulation of said additive in a bio-available form in said plantlet.

1.2 The problem to be solved by the present invention may therefore be regarded as how to fortify pharmaceutical plants with nutrients, minerals or compounds.

1.3 The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) since none of the prior art documents suggests that the plants be subcultured onto a basal medium containing an additive of interest.

2. The subject matter of claim 48 is not new in the sense of Article 33(2) PCT: The plant of claim 48 is defined in terms of a process. Since it is not discernable on the plant how it has been produced, said plant is not rendered novel by the fact that it is produced by means of a new process. A plant grown in nature on soil, which is rich of magnesium for instance, contains more magnesium than a plant grown in absence of magnesium. This was also the case before the earliest priority date of the present application, therefore the subject-matter of claim 48 lacks novelty (Article 33(2) PCT).

3. Claims 1-48 are considered to be industrially applicable (Article 33(4) PCT).

Ad VIII

1. Although claims 1 and 45 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.
   Hence, claims 1 and 45 do not meet the requirements of Article 6 PCT.

2. The present set of dependent claims lacks conciseness (Article 6 PCT) since the subject matter of dependent claims 6, 8, 12-14, 19-21, 23, 25-28, 32-35, 37, 39-41, 44 and 47 is a repetition of the subject-matter of other dependent claims.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION RELATING TO PRIORITY CLAIM

(PCT Rules 26bis.1 and 26bis.2 and Administrative Instructions, Sections 402 and 409)

To:

SECHLEY, Konrad, A.
Gowling, Strathy & Henderson
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

Date of mailing (day/month/year) 22 May 2000 (22.05.00)	
Applicant's or agent's file reference 08-882993WO	**IMPORTANT NOTIFICATION**
International application No. PCT/CA00/00305	International filing date (day/month/year) 24 March 2000 (24.03.00)
Applicant UNIVERSITY OF GUELPH et al	

The applicant is hereby **notified** of the following in respect of the priority claim(s) made in the international application.

1. [X] **Correction of priority claim.** In accordance with the applicant's notice received on: 19 April 2000 (19.04.00), the following priority claim has been corrected to read as follows:

US 27 August 1999 (27.08.99) 60/151,045

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

2. [ ] **Addition of priority claim.** In accordance with the applicant's notice received on: , the following priority claim has been added:

- [ ] even though the indication of the number of the earlier application is missing.
- [ ] even though the following indication in the priority claim is not the same as the corresponding indication appearing in the priority document:

3. [ ] As a **result of the correction and/or addition** of (a) priority claim(s) under items 1 and/or 2, the (earliest) priority date is:

4. [ ] **Priority claim considered not to have been made.**

- [ ] The applicant failed to respond to the Invitation under Rule 26bis.2(a) (Form PCT/IB/316) within the prescribed time limit.
- [ ] The applicant's notice was received after the expiration of the prescribed time limit under Rule 26bis.1(a).
- [ ] The applicant's notice failed to correct the priority claim so as to comply with the requirements of Rule 4.10.

The applicant may, before the technical preparations for international publication have been completed and subject to the payment of a fee, request the International Bureau to publish, together with the international application, information concerning the priority claim. See Rule 26bis.2(c) and the PCT Applicant's Guide, Volume I, Annex B2(IB).

5. [X] In case where **multiple priorities** have been claimed, the above item(s) relate to the following priority claim(s):

US 27 August 1999 (27.08.99) 60/151,045

6. A copy of this notification has been sent to the receiving Office and

- [X] to the International Searching Authority (where the international search report has not yet been issued).
- [X] the designated Offices (which have already been notified of the receipt of the record copy).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Anman QIU
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

003299650

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 11 December 2000 (11.12.00)	
International application No. PCT/CA00/00305	**Applicant's or agent's file reference** 08-882993WO
International filing date (day/month/year) 24 March 2000 (24.03.00)	**Priority date** (day/month/year) 25 March 1999 (25.03.99)
Applicant SAXENA, Praveen, K. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 October 2000 (13.10.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer F. Baechler
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

CA0000305

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
08-882993WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 00/ 00305	24/03/2000	25/03/1999
Applicant		
UNIVERSITY OF GUELPH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]/CA 00/00305

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01H4/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STOJAKOWSKA, A.: "Production of parthenolide in organ cultures of feverfew" PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973 page 160, left-hand column, paragraph 2 -right-hand column, paragraph 1 --- -/--	1-15, 37-47,54

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 September 2000	10/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Fonts Cavestany, A

2

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 5 869 340 A (SHETTY KALIDAS) 9 February 1999 (1999-02-09) column 2, line 28 - line 37 column 4, line 22 - line 26 column 4, line 39 - line 54 column 6, line 57; claim 67 column 7, line 1 - line 3	1,37,46, 58,61 4-8,38, 40-46, 48, 51-53, 56,57, 59,60
X	SUCHITRA BANERJEE: "In vitro multiplication of Centella asiatica, a medicinal herb from leaf explants" CURRENT SCIENCE, vol. 76, no. 2, 25 January 1999 (1999-01-25), pages 147-148, XP000937832	1,2,37, 38,46,47
A	the whole document	58,59
X	BRUTOVSKA ET AL.: "Cytogenetic variability of in vitro regenerated Hypericum perforatum L. plants and their seed progenies" PLANT SCIENCE, vol. 133, 1998, pages 221-229, XP000938218 page 222, left-hand column, paragraph 2 -right-hand column, paragraph 1	1-6,9
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN PREV198681111581, 1986 NORTON: "In-vitro propagation of Ericaceae; a comparison of the activity of the cytokinins (..) in shoot proliferation" XP002148178 & Scientia Horticulturae, Vol. 27, pgs 335-340 abstract	1-61
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN: PREV199799669306, 1997 COCKER ET AL.: "In vitro culture of Echinacea purpurea" XP002148179 & Phytopatology, Vol 87 pag S111 (Meeting of the American Phytopathological Society, March 22-26 1997) abstract	

2

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
/CA 00/00305

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5869340 A	09-02-1999	CA 2246690 A	02-07-1998

PC[redacted]

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No. PCT / C[redacted] 0/00305

International Filing Date 24 MAR 2000 (24.03.00)

Name of receiving Office and "PCT International Application" RO/CA

Applicant's or agent's file reference *(if desired) (12 characters maximum)* O8-882993WO

Box No. I TITLE OF INVENTION

Micropropagation And Preparation Of Phytopharmaceutical Plants

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

University of Guelph
Reynolds Building
Suite 213
Office of Research
Guelph, Ontario
CANADA N1G 2W1

☐ This person is also inventor.

Telephone No.
(519) 824-4120

Facsimile No.
(519) 821-5236

Teleprinter No.

State (that is, *country*) of nationality: CA

State (that is, *country*) of residence: CA

This person is applicant for the purposes of: ☐ all designated states ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SAXENA, Praveen K
32 Fieldstone Road
Guelph, Ontario
CANADA N1L 1B4

This person is:
☐ applicant only
☒ applicant and inventor
☐ inventor only *(If this check-box is marked, do not fill in below.)*

State (that is, *country*) of nationality: CA

State (*that is, country*) of residence: CA

This person is applicant for the purposes of: ☐ all designated states ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

SECHLEY, Konrad A.; ERRATT, Judy A.; DUDLEY, Bruce; MORGAN, Bruce E.; STRAZNICKY, Ivan; D'IORIO, Hélène; O'NEILL, Gary;
Gowling, Strathy & Henderson
Suite 2600, 160 Elgin Street
Ottawa, Ontario
Canada K1P 1C3

Telephone No.
(613) 233-1781

Facsimile No.
(613) 563-9869

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

MURCH, Susan J.
43 William Street
Cambridge, Ontario
CANADA N3H 3W6

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (*If this check-box is marked, do not fill in below.*)

State (that is, *country*) of nationality: CA

State (that is, *country*) of residence: CA

This person is applicant for the purposes of:
- ☐ all designated states
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

KRISHNARAJ, Sankaran
128-78 College Avenue West
Guelph, Ontario
CANADA N1G 4S7

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (*If this check-box is marked, do not fill in below.*)

State (that is, *country*) of nationality: CA

State (that is, *country*) of residence: CA

This person is applicant for the purposes of:
- ☐ all designated states
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SLIMMON, Tannis Y.
71 Grange Street
Guelph, Ontario
CANADA N1E 2V1

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (*If this check-box is marked, do not fill in below.*)

State (*that is, country*) of nationality: CA

State (*that is, country*) of residence: CA

This person is applicant for the purposes of:
- ☐ all designated states
- ☐ all designated States except the United States of America
- ☒ the United States of America only
- ☐ the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only (*If this check-box is marked, do not fill in below.*)

State (*that is, country*) of nationality:

State (*that is, country*) of residence:

This person is applicant for the purposes of:
- ☐ all designated states
- ☐ all designated States except the United States of America
- ☐ the United States of America only
- ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (*mark the applicable check-boxes; at least one must be marked*):

Regional Patent

☒ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, UG Uganda, ZW Zimbabwe and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senagal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (*if other kind of protection or treatment desired, specify on dotted line*).....

National Patent (*if other kind of protection or treatment desired, specify on dotted line*):

☒ **AE** United Arab Emirates
☒ **AL** Albania
☒ **AM** Armenia
☒ **AT** Austria
☒ **AU** Australia
☒ **AZ** Azerbaijan
☒ **BA** Bosnia and Herzegovina
☒ **BB** Barbados
☒ **BG** Bulgaria
☒ **BR** Brazil
☒ **BY** Belarus
☒ **CA** Canada
☒ **CH and LI** Switzerland and Liechtenstein
☒ **CN** China
☒ **CR** Costa Rica
☒ **CU** Cuba
☒ **CZ** Czech Republic
☒ **DE** Germany
☒ **DK** Denmark
☒ **DM** Dominica
☒ **EE** Estonia
☒ **ES** Spain
☒ **FI** Finland
☒ **GB** United Kingdom
☒ **GD** Grenada
☒ **GE** Georgia
☒ **GH** Ghana
☒ **GM** Gambia
☒ **HR** Croatia
☒ **HU** Hungary
☒ **ID** Indonesia
☒ **IL** Israel
☒ **IN** India
☒ **IS** Iceland
☒ **JP** Japan
☒ **KE** Kenya
☒ **KG** Kyrgyzstan
☒ **KP** Democratic People's Republic of Korea
☒ **KR** Republic of Korea
☒ **KZ** Kazakstan
☒ **LC** Saint Lucia
☒ **LK** Sri Lanka
☒ **LR** Liberia
☒ **LS** Lesotho
☒ **LT** Lithuania
☒ **LU** Luxembourg
☒ **LV** Latvia
☒ **MA** Morocco
☒ **MD** Republic of Moldova
☒ **MG** Madagascar
☒ **MK** The former Yugoslav Republic of Macedonia
☒ **MN** Mongolia
☒ **MW** Malawi
☒ **MX** Mexico
☒ **NO** Norway
☒ **NZ** New Zealand
☒ **PL** Poland
☒ **PT** Portugal
☒ **RO** Romania
☒ **RU** Russian Federation
☒ **SD** Sudan
☒ **SE** Sweden
☒ **SG** Singapore
☒ **SI** Slovenia
☒ **SK** Slovakia
☒ **SL** Sierra Leone
☒ **TJ** Tajikistan
☒ **TM** Turkmenistan
☒ **TR** Turkey
☒ **TT** Trinidad and Tobago
☒ **TZ** Tanzania
☒ **UA** Ukraine
☒ **UG** Uganda
☒ **US** United States of America
☒ **UZ** Uzbekistan
☒ **VN** Viet Nam
☒ **YU** Yugoslavia
☒ **ZA** South Africa
☒ **ZW** Zimbabwe

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

☐
☐

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (*Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving office within the 15-month time limit.*)

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application country	regional application:* regional Office	international application: receiving Office
item (1) 25 March 1999 (25.03.1999)	2,267,012	CA		
item (2) 25 August 1999 (25.08.1999)	60/151,045	US		
item (3)				

☒ The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (*only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office*) identified above as item(s): 1

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*

ISA / EPO

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date (*day/month/year*) Number Country (or regional Office)

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	:	4
description (excluding sequence listing part)	:	55
claims	:	20
abstract	:	1
drawings	:	11
sequence listing part of description	:	
Total number of sheets	:	91

This international application is **accompanied** by the item(s) marked below:

1. ☐ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☒ priority document(s) identified in Box No. VI as item(s): 1 to follow
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganisms or other biological material
8. ☐ nucleoitide and/or amino acid sequence listing in computer readable form
9. ☐ other (*specify*):

Figure of the drawings which should accompany the abstract: 1

Language of filing of the international application: ENGLISH

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Konrad A. Sechley
Patent Agent
Gowling, Strathy & Henderson

For receiving Office use only

1. Date of actual receipt of the purported international application: 24 MAR 2000 (24.03.00)
2. Drawings: ☒ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority specified by the applicant: ISA /
6. ☒ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
SECHLEY, Konrad, A. et al.
Gowling, Lafleur Henderson LLP
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence and Administrative Instructions, Section 601(a))

Date of mailing *(day/month/year)*	06.11.00
Applicant's or agent's file reference: 08-882993WO	**IMPORTANT NOTIFICATION**
International application No.: PCT/CA 00/00305	International filing date *(day/month/year)*: 24/03/2000
Priority date *(day/month/year)*: 25/03/1999	
Applicant: UNIVERSITY OF GUELPH et al.	

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

13/10/2000

2. This date of receipt is:

- [x] the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- [ ] the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- [ ] the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. [ ] **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

[ ] *(If applicable)* This notification confirms the information given by telephone, facsimile transmission or in person on: _____

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	TREUILLET A C Tel. (+49-89) 2399-8861

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

To:

SECHLEY, Konrad, A.
Gowling Lafleur Henderson LLP
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

INFORMATION CONCERNING ELECTED OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

Date of mailing (day/month/year) 11 December 2000 (11.12.00)	
Applicant's or agent's file reference 08-882993WO	**IMPORTANT INFORMATION**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/CA00/00305	24 March 2000 (24.03.00)	25 March 1999 (25.03.99)

Applicant UNIVERSITY OF GUELPH et al

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

   AP :GH,GM,KE,LS,MW,SD,SL,SZ,TZ,UG,ZW
   EP :AT,BE,CH,CY,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
   National :AU,BG,CA,CN,CZ,DE,IL,JP,KP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

   EA :AM,AZ,BY,KG,KZ,MD,RU,TJ,TM
   OA :BF,BJ,CF,CG,CI,CM,GA,GN,GW,ML,MR,NE,SN,TD,TG
   National :AE,AL,AM,AT,AZ,BA,BB,BR,BY,CH,CR,CU,DK,DM,EE,ES,FI,GB,GD,GE,GH,
   GM,HR,HU,ID,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MW,MX,PT,SD,
   SG,SI,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW

3. The applicant is reminded that he must enter the "national phase" **before the expiration of 30 months from the priority date** before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing , if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

   Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

   The entry into the European regional phase is postponed **until 31 months from the priority date** for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:
F. Baechler

Telephone No. (41-22) 338.83.38

3715470

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

To:

SECHLEY, Konrad, A.
Gowling, Strathy & Henderson
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

Date of mailing (day/month/year) 18 May 2000 (18.05.00)	
Applicant's or agent's file reference 08-882993WO	**IMPORTANT NOTIFICATION**
International application No. PCT/CA00/00305	International filing date (day/month/year) 24 March 2000 (24.03.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 25 March 1999 (25.03.99)
Applicant UNIVERSITY OF GUELPH et al	

1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).

2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.

3. An **asterisk(*)** appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

4. The **letters "NR"** appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, **the attention of the applicant is directed** to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date	Priority application No.	Country or regional Office or PCT receiving Office	Date of receipt of priority document
25 Marc 1999 (25.03.99)	2,267,012	CA	26 Apri 2000 (26.04.00)

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Marc Salzman

Telephone No. (41-22) 338.83.38

003296642

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 00/00305

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01H4/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STOJAKOWSKA, A.: "Production of parthenolide in organ cultures of feverfew" PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973 page 160, left-hand column, paragraph 2 -right-hand column, paragraph 1 -/--	1-15, 37-47,54

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 September 2000	10/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fonts Cavestany, A

INTERNATIONAL SEARCH REPORT

Int[illegible]tional Application No
PC[illegible]A 00/00305

C.(Continuation) DOCUMENTS CONSID[illegible] TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 869 340 A (SHETTY KALIDAS) 9 February 1999 (1999-02-09)	1,37,46, 58,61
A	column 2, line 28 - line 37	4-8,38, 40-46, 48, 51-53, 56,57, 59,60
	column 4, line 22 - line 26 column 4, line 39 - line 54 column 6, line 57; claim 67 column 7, line 1 - line 3	
X	SUCHITRA BANERJEE: "In vitro multiplication of Centella asiatica, a medicinal herb from leaf explants" CURRENT SCIENCE, vol. 76, no. 2, 25 January 1999 (1999-01-25), pages 147-148, XP000937832	1,2,37, 38,46,47
A	the whole document	58,59
X	BRUTOVSKA ET AL.: "Cytogenetic variability of in vitro regenerated Hypericum perforatum L. plants and their seed progenies" PLANT SCIENCE, vol. 133, 1998, pages 221-229, XP000938218 page 222, left-hand column, paragraph 2 -right-hand column, paragraph 1	1-6,9
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN PREV198681111581, 1986 NORTON: "In-vitro propagation of Ericaceae; a comparison of the activity of the cytokinins (..) in shoot proliferation" XP002148178 & Scientia Horticulturae, Vol. 27, pgs 335-340 abstract	1-61
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN: PREV199799669306, 1997 COCKER ET AL.: "In vitro culture of Echinacea purpurea" XP002148179 & Phytopatology, Vol 87 pag S111 (Meeting of the American Phytopathological Society, March 22-26 1997) abstract	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 00/00305

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5869340 A	09-02-1999	CA 2246690 A	02-07-1998

ATENT COOPERATION TREA

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

BY: _____

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
Gowling, Lafleur Henderson LLP
Attn. SECHLEY, Konrad, A.
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

Date of mailing *(day/month/year)* 10/10/2000	
Applicant's or agent's file reference 08-882993WO	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/CA 00/ 00305	International filing date *(day/month/year)* 24/03/2000
Applicant UNIVERSITY OF GUELPH et al.	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Irene Rbia-Brand

,TENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
08-882993WO		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/CA 00/ 00305	24/03/2000	25/03/1999
Applicant		
UNIVERSITY OF GUELPH et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [ ] None of the figures.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

INTERNATIONAL SEARCH REPORT

ational Application No
PCT/CA 00/00305

A. CLASSIFICATION OF SUBJECT ER
IPC 7 A01H4/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STOJAKOWSKA, A.: "Production of parthenolide in organ cultures of feverfew" PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973 page 160, left-hand column, paragraph 2 -right-hand column, paragraph 1 --- -/--	1-15, 37-47,54

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 September 2000	10/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fonts Cavestany, A

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	US 5 869 340 A (SHETTY KALIDAS) 9 February 1999 (1999-02-09) column 2, line 28 - line 37 column 4, line 22 - line 26 column 4, line 39 - line 54 column 6, line 57; claim 67 column 7, line 1 - line 3 ---	1,37,46, 58,61 4-8,38, 40-46, 48, 51-53, 56,57, 59,60
X	SUCHITRA BANERJEE: "In vitro multiplication of Centella asiatica, a medicinal herb from leaf explants" CURRENT SCIENCE, vol. 76, no. 2, 25 January 1999 (1999-01-25), pages 147-148, XP000937832	1,2,37, 38,46,47
A	the whole document ---	58,59
X	BRUTOVSKA ET AL.: "Cytogenetic variability of in vitro regenerated Hypericum perforatum L. plants and their seed progenies" PLANT SCIENCE, vol. 133, 1998, pages 221-229, XP000938218 page 222, left-hand column, paragraph 2 -right-hand column, paragraph 1 ---	1-6,9
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN PREV198681111581, 1986 NORTON: "In-vitro propagation of Ericaceae; a comparison of the activity of the cytokinins (..) in shoot proliferation" XP002148178 & Scientia Horticulturae, Vol. 27, pgs 335-340 abstract ---	1-61
A	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; AN: PREV199799669306, 1997 COCKER ET AL.: "In vitro culture of Echinacea purpurea" XP002148179 & Phytopatology, Vol 87 pag S111 (Meeting of the American Phytopathological Society, March 22-26 1997) abstract -----	

INTERNATIONAL SEARCH REPORT

...ation on patent family members

...national Application No
PCT/CA 00/00305

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5869340 A	09-02-1999	CA 2246690 A	02-07-1998

PATENT COOPERATION TREA

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SECHLEY, Konrad, A. et al.
Gowling, Lafleur Henderson LLP
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	19.04.01
Applicant's or agent's file reference: 08-882993WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00305	24/03/2000	25/03/1999

Applicant
UNIVERSITY OF GUELPH et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Riebel, O Tel.+49 89 2399-2967

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
08-882993WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00305	24/03/2000	25/03/1999
International Patent Classification (IPC) or national classification and IPC A01H4/00		
Applicant UNIVERSITY OF GUELPH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/10/2000	19.04.01
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Van Woensel, G Telephone No. +49 89 2399 2089

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/00305

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-55	as originally filed				

Claims, No.:

1-49	as received on	21/03/2001	with letter of	19/03/2001	

Drawings, sheets:

1/12-12/12	as originally filed				

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 49.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 49.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-47

	No:	Claims	48
Inventive step (IS)	Yes:	Claims	1-47
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-48
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Ad V

Reference is made to the following document:

D1: STOJAKOWSKA, A.: 'Production of parthenolide in organ cultures of feverfew' PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973

1. The subject-matter of claim 1 meets the requirements of Article 33 PCT: Document D1 discloses a method for the in vitro propagation of *Tanacetum parthenium* comprising, culturing a sterile explant of said plant on an induction medium comprising 6-benzylaminopurine and transferring said regenerated tissue to a basal medium and culturing to form plantlets.

1.1 Document D1 does not disclose that the plantlets are subcultured onto a basal medium containing at least one additive of interest to allow uptake and accumulation of said additive in a bio-available form in said plantlet.

1.2 The problem to be solved by the present invention may therefore be regarded as how to fortify pharmaceutical plants with nutrients, minerals or compounds.

1.3 The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT) since none of the prior art documents suggests that the plants be subcultured onto a basal medium containing an additive of interest.

2. The subject matter of claim 48 is not new in the sense of Article 33(2) PCT: The plant of claim 48 is defined in terms of a process. Since it is not discernable on the plant how it has been produced, said plant is not rendered novel by the fact that it is produced by means of a new process. A plant grown in nature on soil, which is rich of magnesium for instance, contains more magnesium than a plant grown in absence of magnesium. This was also the case before the earliest priority date of the present application, therefore the subject-matter of claim 48 lacks novelty (Article 33(2) PCT).

3. Claims 1-48 are considered to be industrially applicable (Article 33(4) PCT).

Ad VIII

1. Although claims 1 and 45 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness. Moreover, lack of clarity of the claims as a whole arises, since the plurality of independent claims makes it difficult, if not impossible, to determine the matter for which protection is sought, and places an undue burden on others seeking to establish the extent of the protection.
   Hence, claims 1 and 45 do not meet the requirements of Article 6 PCT.

2. The present set of dependent claims lacks conciseness (Article 6 PCT) since the subject matter of dependent claims 6, 8, 12-14, 19-21, 23, 25-28, 32-35, 37, 39-41, 44 and 47 is a repetition of the subject-matter of other dependent claims.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A method for the *in vitro* micropropagation and phytofortification of a phytopharmaceutical plant comprising:

a) culturing a sterile explant of said phytopharmaceutical plant on an induction medium comprising at least one plant growth regulator having cytokinin activity, to form regenerated tissue;

b) transferring said regenerated tissue to a basal medium and culturing to form plantlets; and

c) subculturing said plantlets onto a basal medium containing at least one additive of interest, to allow uptake and accumulation of said at least one additive of interest in a bio-available form in said plantlet.

2. The method of claim 1, wherein after said step of culturing (step a)), and prior to said step of transferring (step c)), said regenerated tissue is placed on a basal medium and subcultured to allow optimized formation of regenerated tissue; and

3. The method of claim 1 wherein after said step of transferring (step b)), said plantlet is transferred to a hydroponic environment with a recycling solution containing at least one additive of interest to allow uptake and accumulation of said at least one additive of interest in a bioavailable form within said plantlet or seedling.

4. The method according to any one of claim 1, 2 or 3, wherein in said culturing step, said at least one additive of interest is selected from boron, calcium, chloride, chromium, cobalt, copper, iron, lithium, iodine, magnesium, manganese, molybdenum, nickel, phosphorous, potassium, selenium, silicon, sodium, sulphur, tin, vanadium and zinc.

5. The method of any one of claims 1 to 4, wherein said phytopharmaceutical plant is selected from the group consisting of:

Achillea millefolium

Achyranthes bidentata

Aconitum napellus

Adonis aestivalis

Agastache mexicana

Agrimonia eupatoria

Agathosma betulina

Allium sp

Anchusa officinalis

Anemopsis californica

Angelica dahurica

Angelica polymorpha sinensis (A. sinensis)

Arnica Montana

Ammi visnaga

Arctostaphylos uva-ursi

Asclepias tuberosa

Astragalus membranaceus

Astragalus chinensis

Baphicacanthus cusia

Bixa orellana

Bupleurum falcatum

Brugmansia (Datura) spp.

Campanula rapunculus

Carum roxburgianum

Carum copticum

Cassia tora

Chamaelirium luteum

Chimaphila umbellata

Commiphora africana

Conium maculatum

Crithium maritimum

Datura metel (Datura alba)

Datura inoxia

Dracocephalum moldavica

Echinacea sp.

Eclipta alba (E. prostrata)

Ephedra nevadensis

Eriodictyon californicum

Eucommia ulmoides

Eupatorium perfoliatum

Filipendula vulgaris (F. hexapetala)

Gaultheria procumbens

Geum urbanum

Houttuynia cordata

Hydrocotyle asiatica (Centella asiatica)

Hypericum perforatum cv. Anthos

Inula helenium

Jatropha curcas

Leptospermum scoparium

Lespedeza capitata

Ligusticum porteri

Ligustrum lucidum

Lithospermum officinale

Lycium barbarum

Mucuna pruriens

Mandragora officinarum

Origanum dictamnus

Parietaria judaica (P. officinalis)

Phyllanthus emblica

Picrasma excelsa

Piniella ternate

Pogostemon patchouli

Polygonum multiflorum

Porophyllum ruderale ssp. macrocephalum

Prunella vulgaris

Pueraria lobata (P. thunbergiana)

Rauvolfia serpentina

Rivea corymbosa

Sanguinaria Canadensis
Satureja douglasii
Schizonepeta tenuifolia
Scutellaria baicalensis
Solanum xanthocarpum (S. surattense)
Sutherlandia frustescens
Tabebuia impetiginosa
Tanacetum parthenium
Tribulus terrestris
Trichosanthes kirilowii
Turnera diffusa
Voacanga africana, and
Withania somnifera

6. The method according to claim 5, wherein said phytopharmaceutical plant is selected from St. John's wort (*Hypericum perforatum* cv. Anthos), Huang-qin (*Scutellaria baicalensis*), *Echinacea sp.* and feverfew (*Tanacetum parthenium*).

7. The method according to any one of claims 1 to 6, wherein said at one plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron (TDZ, *N*-phenyl-*N'*-(1,2,3-thidiazol-yl)urea), benzylaminopurine (BAP), zeatin, CPPU (N-(2-chloro-4pyridyl)-N(-phenyl urea) and 2-*i*-P (N6-(2-isopentenyl) adenine or 6-gamma,gamma-dimethylallylamino purine).

8. The method according to claim 7, wherein said at least one plant growth regulator having cytokinin activity is selected from thidiazuron (TDZ) and benzylaminopurine (BAP).

9. The method according to claim 8, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said at least plant growth regulator having cytokinin activity.

10. The method according to claim 8, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

11. The method according to any one of claims 1 to 10, wherein said explant is selected from the seed, petiole, hypocotyl, stem, cotyledon and leaf.

12. The method according to any one of claims 1 to 4, wherein said phytopharmaceutical plant is St. John's wort.

13. The method according to claim 12, wherein said plant growth regulator having cytokinin activity is thidiazuron.

14. The method according to claim 13, wherein the induction medium comprises thiadiazuron from about 0.001 to about 25 $\mu mol \cdot L^{-1}$.

15. The method according to claim 14, wherein the induction medium comprises thiadiazuron from about 4 to about10 $\mu mol \cdot L^{-1}$.

16. The method according to claim 12, wherein said sterile explant is maintained on said induction medium from about 1 to about 15 days.

17. The method according to claim 16, wherein said sterile explant is maintained on said induction medium from about 8 to about 10 days.

18. The method according to claim 12, wherein said explant is etiolated hypocotyl.

19. The method according to any one of claims 1 to 4, wherein the phytopharmaceutical plant is *Echinacea sp.*.

20. The method according to claim 19, wherein said plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron and benzylaminopurine.

21. The method according to claim 20, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said plant growth regulator having cytokinin activity.

22. The method according to claim 20, wherein said plant growth regulator having cytokinin activity is from about 1.0 to about 15 $\mu mol \cdot L^{-1}$.

23. The method according to claim 19, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

24. The method according to claim 23, wherein said sterile explant is maintained on said induction medium from about 10 to about 35 days.

25. The method according to claim 19, wherein said explant is petiole.

24. The method according to any one of claims 1 to 4, wherein said phytopharmaceutical plant is Huang qin.

27. The method according to claim 26, wherein said plant growth regulator having cytokinin activity is thidiazuron.

28. The method according to claim 27, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said plant growth regulator having cytokinin activity.

29. The method according to claim 28, wherein said plant growth regulator having cytokinin activity is from about 1.5 to about 20 $\mu mol \cdot L^{-1}$

30. The method according to claim 26, wherein said sterile explant is maintained on said induction medium from about 1 to about 30 days.

31. The method according to claim 30, wherein said sterile explant is maintained on said induction medium from about 14 to about 20 days.

32. The method according to claim 26, wherein said explant is selected from seeds, hypocotyl and stems.

33. The method according to any one of claims 1 to 4, wherein the phytopharmaceutical plant is feverfew.

34. The method according to claim 33 wherein said plant growth regulator having cytokinin activity is thidiazuron.

35. The method according to claim 34, wherein said induction medium comprises from about 0.001 to about 25 $\mu mol \cdot L^{-1}$ of said plant growth regulator having cytokinin activity.

36. The method according to claim 35, wherein said plant growth regulator having cytokinin activity is from about 2.0 to about 8.0 $\mu mol \cdot L^{-1}$

37. The method according to claim 33, wherein said sterile explant is maintained on said induction medium from about 1 to about 50 days.

38. The method according to claim 37, wherein said sterile explant is maintained on said induction medium from about 20 to about 35 days.

39. The method according to claim 33, wherein the explant is selected from leaf, stem, petiole and hypocotyl.

40. The method according to claim 4, wherein said at least one additive of interest is zinc.

41. A method according to claim 4, wherein said at least one additive of interest is lithium.

42. The method according to claim 4, wherein said at least one additive of interest within said basal medium, is from about 0.001 to about 500 $mg \cdot L^{-1}$.

44. The method according to claim 2, wherein, in said transferring step, said regenerated tissue is subcultured for about 1 to about15 days.

45 A method for phytofortification of an *in vitro*-grown phytopharmaceutical plant comprising:

a) culturing a sterile seedling, explant or regenerated tissues to form a plantlet; and

b) subculturing said plantlet onto a basal medium containing at least one additive of interest, to allow uptake and accumulation of said at least one additive of interest in a bio-available form in said plantlet.

46. The method according to claim 45, wherein, in said step of culturing, said plantlets are produced either:

a) on a sterile explant of said phytopharmaceutical plant grown on an induction medium comprising at least one plant growth regulator having cytokinin activity, or

b) grown from a sterile seed, or

c) seedling in culture.

47. The method according to claim 46, wherein said at one plant growth regulator having cytokinin activity is selected from the group consisting of thidiazuron (TDZ, *N*-phenyl-*N'*-(1,2,3-thidiazol-yl)urea), benzylaminopurine (BAP), zeatin, CPPU (N-(2-chloro-4pyridyl)-N(-phenyl urea) and 2-*i*-P (N6-(2-isopentenyl) adenine or 6-gamma,gamma-dimethylallylamino purine).

48. A phytopharmaceutical plant prepared by the method of any one claims 1 to 4, or 45 to 47 and comprising an elevated level of said additive of interest when compared to a plant grown in the absence of said additive of interest.

49. A method for the *in vitro* micropropagation involving *de novo* shoot formation of non-meristematic tissue of a phytopharmaceutical plant comprising:

a) culturing a sterile explant of said phytopharmaceutical plant on an induction medium comprising one or more plant growth regulators having cytokinin activity, to form regenerated tissue; and

b) transferring said regenerated tissue to a basal medium and culturing to form plantlets.

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

SECHLEY, Konrad, A. et al.
Gowling, Lafleur Henderson LLP
Suite 2600
160 Elgin Street
Ottawa, Ontario K1P 1C3
CANADA

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	18.12.2000
Applicant's or agent's file reference: 08-882993WO	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/CA00/00305	24/03/2000	25/03/1999

International Patent Classification (IPC) or both national classification and IPC

A01H4/00

Applicant

UNIVERSITY OF GUELPH et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 25/07/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
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I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".)*:

Description, pages:

1-55	as originally filed			

Claims, No.:

1-58	as originally filed			
59-61	as received on	05/06/2000	with letter of	05/06/2000

Drawings, sheets:

1/12-12/12	as received on	05/06/2000	with letter of	05/06/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrialapplicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1,37,61
Inventive step (IS)	Claims	46
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Ad V

Reference is made to the following documents:

D1: STOJAKOWSKA, A.: 'Production of parthenolide in organ cultures of feverfew' PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973

D2: US-A-5 869 340 (SHETTY KALIDAS) 9 February 1999 (1999-02-09)

D3: SUCHITRA BANERJEE: 'In vitro multiplication of Centella asiatica, a medicinal herb from leaf explants' CURRENT SCIENCE, vol. 76, no. 2, 25 January 1999 (1999-01-25), pages 147-148, XP000937832

1. The present application does not meet the requirements of Article 33 PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.
Document D1 discloses a method for the in vitro propagation of *Tanacetum parthenium* comprising, culturing a sterile explant of said plant on an induction medium comprising 6-benzylaminopurine (see abstract) and transferring said regenerated tissue to a basal medium and culturing to form plantlets (see page 160, third paragraph).
Therefore, the subject matter of claim 1 is not novel (Article 33(2) PCT). Also documents D2 (see column 4, lines 15-54 and column 6, line 57 - column 7, line 3) and D3 (see page 147, second column, second paragraph - third column, first paragraph and figs. e and f) destroy the novelty of claim 1.

2.1 The subject-matter of claim 46 meets the requirements of Article 33 PCT:
The above mentioned prior art documents do not disclose that the plantlets are subcultured onto a basal medium containing at least one additive of interest to allow uptake and accumulation of said additive in a bio-available form is said plantlet.

2.2 The problem to be solved by the present invention may therefore be regarded as how to fortify pharmaceutical plants with nutrients, minerals or compounds?

2.3 The solution to this problem proposed in claim 46 of the present application is considered as involving an inventive step (Article 33(3) PCT) since none of the prior art documents suggests that the plants be subcultured onto a basal medium containing an additive of interest.

2.4 Claim 46 is considered to be industrially applicable. Therefore, all requirements of Article 33 PCT have been met.

3. The subject matter of claim 61 is not new in the sense of Article 33(2) PCT: The plant of claim 61 is defined in terms of a process. Since it is not discernable on the plant how it has been produced, said plant is not rendered novel by the fact that it is produced by means of a new process: the plants described in documents D1, D2 and D3 destroy therefore the novelty of claim 61.

Ad VIII

1. In order to meet the requirements of conciseness (Article 6 PCT), it would appear appropriate to file an amended set of claims defining the relevant subject-matter in terms of a single independent method claim (based on the present claim 46) followed by dependent claims covering features which are merely optional (Rule 6.4 PCT).

2. The present set of dependent claims also lacks conciseness (Article 6 PCT) since subject matter of dependent claims (for example subject-matter of claims 2, 4, 6, 7, 8, ...) is repeated several times: For instance, claims 38, 47 and 59 correspond to claim 2, the subject-matter of claim 3 is also disclosed in claim 2, claim 40 corresponds to claim 4, etc.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

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5 October 2000 (05.10.2000)

PCT

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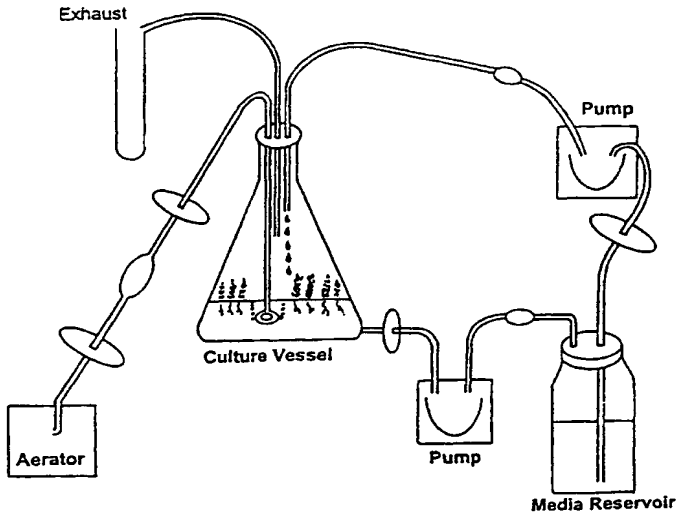
(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: MICROPROPAGATION AND PRODUCTION OF PHYTOPHARMACEUTICAL PLANTS



(57) Abstract: The development of an *in vitro* regeneration system that utilizes a plant growth regulator having cytokinin activity for the induction of *de novo* shoots or somatic embryos on explants of phytopharmaceutical plants is provided. Transfer of the regenerated shoots or somatic embryos into a solid or liquid medium with no plant growth regulators results in the rapid and prolific growth of viable plantlets. The method and its modifications are intended for application to all phytopharmaceutical plants, in particular St.John's wort (*Hypericum perforatum* cv. Anthos), Huang-qin (*Scutellaria baicalensis*), *Echinacea sp.*, Feverfew (*Tanacetum parthenium*), garlic (*Allium sp.*) and the like. Furthermore, a process for the uptake of nutrients, minerals or additives from the growth medium and accumulation of these in the consumable biomass of plants, hereafter referred to as phytofortification, is also described. This process provides additives within a bioavailable form within plants and renders nutrients and additives amenable for easy assimilation by the human of livestock digestive systems.

WO 00/57690 A3

Published:
— *With international search report.*

(88) Date of publication of the international search report:
18 January 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
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DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

[redacted]

In [redacted]al Application No
PCT [redacted] 00/00305

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01H4/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01H

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STOJAKOWSKA, A.: "Production of parthenolide in organ cultures of feverfew" PLANT CELL TISSUE AND ORGAN CULTURE, vol. 47, 1997, pages 159-162, XP000937973 page 160, left-hand column, paragraph 2 -right-hand column, paragraph 1 -/--	1-15, 37-47,54

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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Date of the actual completion of the international search	Date of mailing of the international search report
26 September 2000	10/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fonts Cavestany, A

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X A	US 5 869 340 A (SHETTY KALIDAS) 9 February 1999 (1999-02-09) column 2, line 28 - line 37 column 4, line 22 - line 26 column 4, line 39 - line 54 column 6, line 57; claim 67 column 7, line 1 - line 3	1,37,46, 58,61 4-8,38, 40-46, 48, 51-53, 56,57, 59,60
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